

THE SALK INSTITUTE

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Dear Charlie,

I think I should make more explicit my objection to your chromosome model. This is that there is no evidence to suggest that the "solenoid" type of nucleosome assembly is highly regular. Nothing as regular as TMV, for example, has ever been seen in chromatin and there are very sound reasons to suspect that it cannot be regular. This is because if there has to be this high degree of regularity the axis of the solenoid must be straight. If the solenoid axis were bent or helical then necessarily the packing between nucleosomes in a solenoid will not repeat exactly at each nucleosome. The further the deviation from the straight, the greater the disturbance to the packing.

No one has ever succeeded in proposing successfully a model of a chromosome consisting almost entirely of straight solenoids. The most likely models are those in which the solenoid axis is either bent in a circle or coiled into another helix at a higher level or coiled in an irregular way. The data provided by Laemmli and other evidence suggesting domains in chromosomes, almost demands such a type of super-folding.

For these reasons I think that the packing of nucleosomes into a solenoid is not a highly precise one and the variation in the length of DNA per nucleosome also suggests that this is the case. I think it most unlikely that, with this situation, you can have the sort of process you have suggested.

For these reasons I do not merely think that your model may perhaps be wrong. I feel rather strongly that it is highly likely to be wrong! Of course if you can persuade me to change my opinion I would be only too delighted.

See you on Thursday,

Yours ever, Francis

FHCC/hm1

F. H. C. Crick